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GUEST EDITORIAL

New Screening Guidelines for Colorectal Cancer

WILLIAM L. DONEGAN, MD*
Department of Surgery, Medical College of Wisconsin, Milwaukee, Wisconsin

Colorectal cancer is second only to lung cancer as a cause of death from cancer in the United States. It accounts for 131,200 new cases of cancer and claims about 55,000 lives per year, a burden shared equally by men and women [1]. The majority of these deaths are preventable. From what is presently known about the natural history of colorectal cancer, it is clear that an opportunity exists not only to prevent this disease but to preempt its lethal phase. The key is the evolution known as the adenoma to carcinoma sequence. The great majority of colorectal cancers originate from the mucosa of the large bowel as adenomatous polyps. As adenomatous polyps enlarge, they become dysplastic and undergo malignant change, which is followed by invasion and metastasis [2]. The evolution to malignancy is marked by a succession of genetic mutations that act to disable tumor suppressor genes, disrupt DNA mismatch repair genes, and in turn alter other genetic regulators of cell growth, typically K-ras, DCC and p53 [3]. In most cases this begins as a somatic mutation. Of individuals with colorectal carcinoma, 5–10% carry genetic mutations in their germ line that predispose to this disease [4]. The family members of these persons are at especially high risk. Hereditary colorectal cancer often develops at an early age and in some instances is preceded by myriads of adenomatous polyps in the large bowel. The malignant polyp phenotypes include familial adenomatous polyposis (FAP), Gardner syndrome, and Turcot syndrome. A more recently recognized familial form, hereditary nonpolyposis colorectal carcinoma (HNPCC), can develop without polyps but has identifiable clinical features, i.e., early onset, multiple cancers, and a tendency for cancers to involve the right side of the colon. The several years required for polyps to progress to malignancy offers a window of opportunity to discover and remove the polyps and prevent the development of malignancy [5]. Even after malignant change has occured, ample chance for cure remains. Colorectal cancers found while asymptomatic are more often localized than those found after symptoms have developed. If colorectal cancers are found while they are still confined to the bowel wall (TNM Stage I), resection is associated with a highly favorable prognosis; 5-yr relative survival rates are regularly 70% or greater [6].

The major problem with screening for colorectal cancer is that the large bowel is not easily examined. Digital examination of the rectum (DRE) is time honored, safe, and inexpensive, but only ~5% of cancers are within finger reach. Fecal occult blood testing (FOBT) can detect cancers that bleed, but the examination is nonspecific. Cancers bleed inconsistently and other lesions bleed as well. For these reasons FOBT is plagued with false positive (2–3%) and false negative (22–58%) test results [5]. Flexible sigmoidoscopy has a decided advantage in reach over rigid sigmoidoscopy for direct surveillence of the rectum and distal sigmoid colon, or as a complement to double (air) contrast barium enema (DCBE), but as a solitary measure flexible sigmoidoscopy leaves most of the colon unexamined. Examination of the whole colon requires either DCBE or flexible colonoscopy, both of which are uncomfortable and expensive and require preliminary purging of the intestine. Double contrast barium enema involves 300–500 mrem of radiation exposure and offers neither the ability to biopsy lesions nor to remove polyps. If a lesion is discovered, a second examination with colonoscopy may be necessary. Colonoscopy offers the convenience of examination and biopsy or polyp removal, but it is considerably more expensive than DCBE, usually requires sedation, and accidental perforation of the bowel is estimated to occur in 1 of every 1,000 examinations. Each 10,000 examinations cause 1–3 deaths [7]. If the cecum is not reached, a DCBE may be required as well. Even at bargain prices,

*Correspondence to: William L. Donegan, MD, Department of Surgery, Sinai Samaritan Medical Center, 950 N. 12th Street, Milwaukee, WI 53201. Telephone No. : (414) 219-6809; Fax No.: (414) 219-734. E-mail: wilado@aol.com

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colonoscopy, or for that matter screening for colorectal cancer in general, is not embraced by the public with any enthusiasm.

Despite these caveats, the evidence is compelling that regular screening can reduce deaths from colorectal cancer [7–9]. Three case control studies of sigmoidoscopy have demonstrated that regular examinations reduce mortality from rectal cancer. Five controlled trials of regular FOBT followed by DCBE or endoscopic investigation of persons with positive tests have been reported; colorectal cancer mortality was reduced by 15–33%. A trial of routine FOBT plus sigmoidoscopy indicated that the combination was more effective in reducing deaths from colorectal cancer than sigmoidoscopy alone. The crucial decisions about screening are whom to screen, how often, and with what.

The American Cancer Society (ACS) has advocated screening of asymptomatic individuals for colorectal cancer for the last 40 yr and has periodically updated the recommendations in response to new knowledge and technology. Originally a DRE, proctoscopic examination, and FOBT at the time of an annual health checkup was advised for all persons > 40 yr of age. In 1980, a better understanding of the role of polyps in carcinogenesis and the time required for the transformation to malignancy to occur caused the recommendations to be scaled back [10]. Annual FOBT and rigid sigmoidoscopy were deferred until after age 50, and the frequency of sigmoidoscopy was reduced to every 3–5 yr after two negative examinations 1 yr apart. At this point flexible sigmoidoscopy was considered ''too expensive and specialized'' to be used for early detection. The continued development of flexible endoscopy made not only the rectum but the entire colon readily accessible to direct visualization, and specialized instrumentation permitted biopsy and polyp removal via the endoscope. In 1992, the American Cancer Society responded accordingly [11]. Flexible sigmoidoscopy was recommended in preference to rigid sigmoidoscopy, and complete colon examinations were recommended for persons at high risk, i.e., those with a first-degree relative who developed the disease at age 55 or earlier. High risk individuals were advised to begin screening as early as age 35 and to include a colonoscopy or a double contrast barium enema every 5 yr. In the 1990s the important role of genetics in colon cancer has become clearer and so has the need for further refinement of screening strategy. In March of 1997, after extensive review and consultation, the ACS published new screening guidelines for colorectal cancer that are specific for different levels of personal risk [12]. These guidelines recognize both DCBE and colonoscopy as acceptable for total colon examination (TCE) depending on available resources and expertise, and a DRE is advised in conjunction with each sigmoidoscopy or TCE. The new guidelines are as follows:

- Persons at average risk (~70–80% of the population) should begin screening at age 50, and screening should consist of FOBT every year and flexible sigmoidoscopy every 5 yr. TCE should be performed every 10 yr with colonoscopy, or every 5–10 yr with DCBE.
- Persons at moderate risk (an estimated 15–20% of the population) are identified as those with a history of adenomatous polyps, curative resection of colorectal cancer, or colorectal cancer in close relatives. After discovery of adenomatous polyps, a colonoscopy to clear the colon is recommended initially and a follow-up TCE within 3 yr. Provided no further polyps are found, persons who had a single small polyp are followed as average risk; others have a TCE every 5 yr. After curative resection for colorectal cancer TCE is repeated after 1 yr, then after 3 yrs and then after 5 yr. Colorectal cancer or adenomatious polyps in a first-degree relative younger than 60 yr, or in any two first-degree relatives prompts a TCE at age 40 (or 10 yr younger than the youngest affected relative, whichever is earlier), and then every 5 yr.
- Persons at high risk (5–10% of the population) are those with a family history of FAP or HNPCC or who have inflammatory bowel disease. Screening for individuals with FAP begins at puberty and includes endoscopy, counseling, and genetic testing. If polyps or a FAP mutation are found, colectomy is recommended; otherwise endoscopy at 1–2 yr intervals. With a history of HNPCC, screening begins at age 21 and includes colonoscopy, counseling, and genetic testing. With an unknown or positive genetic test, colonoscopy is recommended every 2 yr until age 40 and every 1 yr thereafter. For inflammatory bowel disease, colonoscopies with biopsies for dysplasia are advised beginning 8 yr after the onset of pancolitis or 12–15 yr after the onset of left-sided colitis and should be performed every 1–2 yr.

Screening is a complicated process, and formulating guidelines for screening is also complicated. Guidelines involve decisions about the effectiveness, cost, and risk of interventions, and some arbitrary decisions, such as the age at which screening should begin. For example, why begin at age 50; why not at age 49? For guidelines to have credibility, a consensus should exist about their appropriateness. The ACS made this an important objective. The current ACS guidelines for colorectal cancer screening are comparable to those released in 1996 by the US Preventive Services Task Force and are consistent with those recommended by a task force convened by the Agency for Health Care Policy Research, which was supported by the American Gastroenterological Association, the American Society for Gastrointestinal Endoscopy,

the American College of Gastroenterology, and the American Society of Colon and Rectal Surgeons, among others [7,13].

Guidelines must be recognized as general recommendations for professionals and the public based on the best available current knowledge and judgments. They do not address all circumstances or needs and require continuing evaluation and revision. It is important to appreciate that they do not achieve their purpose by existing. Guidelines that are not used are of no value. The ultimate objective is reduced morbidity and mortality from cancer, and to achieve this goal they must be placed into practice and combined with appropriate treatment. As ephemeral as guidelines may be, they are a valuable resource for primary care and specialty physicians who seek to provide informed care.

REFERENCES

1. Cancer Facts and Figures 1997. American Cancer Society, 1599 Clifton Road, NE, Atlanta,GA 30329-4251.
2. Madoff RD: Colorectal cancer genetics. Bull Am College Surgeons 1996;81:26–32.
3. Jessup JM, Menck HR, Frengen A, Winchester DP: Diagnosing colorectal carcinoma: Clinical and molecular approaches, CA Cancer J Clin 1997;47:70–92.
4. Watne AL: Colon polyps. J Surg Oncol 1997;66:207–214.
5. DeCosse JJ, Tsioulias GJ, Jacobson JS: Colorectal cancer: Detection, treatment, and rehabilitation. CA Cancer J Clin 1997;44:27–42.
6. Jessup JM, McGinnis LS, Steele GD Jr, et al.: The national cancer data base report on colon cancer. Cancer 1996;78:918–926.
7. Winawer SJ, Fletcher RH, Miller L, et al.: Colorectal cancer screening: Clinical guidelines and rationale. Gastroenterology 1997;112:594–642.
8. Selby JV, Friedman GD, Quesenberry CP Jr, Weiss NS: A case-control study of screening sigmoidscopy and mortality from colorectal cancer. N Engl J Med 1992;326:653–657.
9. Mandel JS, Bond JH, Church TR, et al.: Reducing mortality from colorectal cancer by screening for fecal occult blood: Minnesota Colon Cancer Control Study. N Engl J Med 1993;328:1467–1471.
10. Cancer of the Colon and Rectum. CA Cancer J Clin 1980; 30: 208–215.
11. Levin B, Murphy GP: Revisions in American Cancer Society recommendations for the early detection of colorectal cancer. CA Cancer J Clin 1992;42:296–299.
12. Byers T, Levin B, Rothenberger D, et al.: American Cancer Society guidelines for screening and surveillance for early detection of colorectal polyps and cancer: Update 1997. CA Cancer J Clin 1997;47:154–160.
13. U.S. Preventive Services Task Force: Guide to Clinical Preventive Services: Report of the LU.S. Preventive Services Task Force, ed 2. Washington, DC: Government Printing Office, 1996.